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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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10/070,295

09/09/2002

Menachem Rubinstein

RUBINSTEIN=7

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EXAMINER

CHANDRA, GYAN

ART UNIT

PAPER NUMBER

1646

MAIL DATE

DELIVERY MODE

04/10/2009

PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

<p align="center">Advisory Action Before the Filing of an Appeal Brief</p>	Application No. 10/070,295	Applicant(s) RUBINSTEIN ET AL.	
	Examiner GYAN CHANDRA	Art Unit 1646	

--The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

THE REPLY FILED 01 April 2009 FAILS TO PLACE THIS APPLICATION IN CONDITION FOR ALLOWANCE.

1. ☒ The reply was filed after a final rejection, but prior to or on the same day as filing a Notice of Appeal. To avoid abandonment of this application, applicant must timely file one of the following replies: (1) an amendment, affidavit, or other evidence, which places the application in condition for allowance; (2) a Notice of Appeal (with appeal fee) in compliance with 37 CFR 41.31; or (3) a Request for Continued Examination (RCE) in compliance with 37 CFR 1.114. The reply must be filed within one of the following time periods:

- a) ☒ The period for reply expires 3 months from the mailing date of the final rejection.
b) ☐ The period for reply expires on: (1) the mailing date of this Advisory Action, or (2) the date set forth in the final rejection, whichever is later. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of the final rejection.

Examiner Note: If box 1 is checked, check either box (a) or (b). ONLY CHECK BOX (b) WHEN THE FIRST REPLY WAS FILED WITHIN TWO MONTHS OF THE FINAL REJECTION. See MPEP 706.07(f).

Extensions of time may be obtained under 37 CFR 1.136(a). The date on which the petition under 37 CFR 1.136(a) and the appropriate extension fee have been filed is the date for purposes of determining the period of extension and the corresponding amount of the fee. The appropriate extension fee under 37 CFR 1.17(a) is calculated from: (1) the expiration date of the shortened statutory period for reply originally set in the final Office action; or (2) as set forth in (b) above, if checked. Any reply received by the Office later than three months after the mailing date of the final rejection, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

NOTICE OF APPEAL

2. ☐ The Notice of Appeal was filed on _____. A brief in compliance with 37 CFR 41.37 must be filed within two months of the date of filing the Notice of Appeal (37 CFR 41.37(a)), or any extension thereof (37 CFR 41.37(e)), to avoid dismissal of the appeal. Since a Notice of Appeal has been filed, any reply must be filed within the time period set forth in 37 CFR 41.37(a).

AMENDMENTS

3. ☐ The proposed amendment(s) filed after a final rejection, but prior to the date of filing a brief, will not be entered because
(a) ☐ They raise new issues that would require further consideration and/or search (see NOTE below);
(b) ☐ They raise the issue of new matter (see NOTE below);
(c) ☐ They are not deemed to place the application in better form for appeal by materially reducing or simplifying the issues for appeal; and/or
(d) ☐ They present additional claims without canceling a corresponding number of finally rejected claims.

NOTE: _____. (See 37 CFR 1.116 and 41.33(a)).

4. ☐ The amendments are not in compliance with 37 CFR 1.121. See attached Notice of Non-Compliant Amendment (PTOL-324).
5. ☐ Applicant's reply has overcome the following rejection(s): _____.
6. ☐ Newly proposed or amended claim(s) _____ would be allowable if submitted in a separate, timely filed amendment canceling the non-allowable claim(s).
7. ☐ For purposes of appeal, the proposed amendment(s): a) ☐ will not be entered, or b) ☐ will be entered and an explanation of how the new or amended claims would be rejected is provided below or appended.
The status of the claim(s) is (or will be) as follows:
Claim(s) allowed: _____.
Claim(s) objected to: _____.
Claim(s) rejected: _____.
Claim(s) withdrawn from consideration: _____.

AFFIDAVIT OR OTHER EVIDENCE

8. ☐ The affidavit or other evidence filed after a final action, but before or on the date of filing a Notice of Appeal will not be entered because applicant failed to provide a showing of good and sufficient reasons why the affidavit or other evidence is necessary and was not earlier presented. See 37 CFR 1.116(e).
9. ☐ The affidavit or other evidence filed after the date of filing a Notice of Appeal, but prior to the date of filing a brief, will not be entered because the affidavit or other evidence failed to overcome all rejections under appeal and/or appellant fails to provide a showing a good and sufficient reasons why it is necessary and was not earlier presented. See 37 CFR 41.33(d)(1).
10. ☐ The affidavit or other evidence is entered. An explanation of the status of the claims after entry is below or attached.

REQUEST FOR RECONSIDERATION/OTHER

11. ☒ The request for reconsideration has been considered but does NOT place the application in condition for allowance because: see continuation sheet.
12. ☐ Note the attached Information *Disclosure Statement*(s). (PTO/SB/08) Paper No(s). _____.
13. ☐ Other: _____.

/Robert Landsman/
Primary Examiner, Art Unit 1647

Continuation of 11 does not place the application in condition for allowance because:

Applicant's response filed on 4/01/2009 is acknowledged and fully considered.

Status of Application, Amendments, And/Or Claims

Claims 5, 9, 11, 12, 15-17 and 19 are pending and examination on the merit to the extent that they read on the elected invention of VEGF inhibitor – CSC.

Response to Arguments

Claim Rejections-maintained

Claim Rejections - 35 USC § 112-enablement

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 5, 9, 11, 12, 15-17 and 19 stand rejected under 35 U.S.C. 112, first paragraph-enablement for the reasons of record in pg. 5-10 of the Office Action of 2/13/2006, in pg. 3-5 of the Office Action of 4/5/2007, in pg. 3-6 of the Office Action of 10/7/2008, and in pg. 2-4 of the Office Action of 1/30/2009.

The instant claims are drawn to a method for inhibiting angiogenesis in adipose tissues in mammals comprising administering to a subject a pharmaceutical composition comprising (i) leptin, (ii) a leptin fragment, (iii) a leptin homolog having 90% sequence identity with sequence of leptin, or (iv) a derivative of leptin or leptin homolog which has the activity of leptin, and optionally, an inhibitor of angiogenesis in a suitable dosage, (v) wherein angiogenesis inhibitor is a VEGF inhibitor, (vi) wherein the derivative said derivative has one or more chemical moieties attached to leptin, (vii) wherein said chemical moieties are water soluble polymers, wherein said polymers are polyethylene glycol, and wherein VEGF is absent in the adipose tissue.

Applicants argue (pg. 2-3 of Response) that Figure 7 and Example 7 (pages 27-28) of the instant specification show that the adipose tissue of normal mice contain very low levels of VEGF and this remains the same even after leptin administration. Applicants argue that in the absence of VEGF Ang-2 is angiostatic and that one skilled in the art would think that leptin is also angiostatic in the absence of VEGF.

Applicants' arguments have been fully considered but they are not found persuasive because the instant claims are not directed to leptin being angiostatic in the absence of VEGF in adipose tissue rather the claims are directed to a method of inhibiting angiogenesis in adipose tissue in mammals comprising administering leptin. The art has established that the administration of leptin promotes wound healing which requires angiogenesis (previously presented, Frank et al, J. Clin. Invest. 106: 501-509, 2000; Sierra-Honigmann (U.S. Pub. No. 2007/0275874 A1) and that leptin promotes angiogenesis in pre-adipocyte of normal mammal (previously presented, Park et al), one skill in the art would not conclude the role of leptin as an angiogenic inhibitor in adipose tissue of normal mammals, unless evidence to contrary. Because the disclosure is devoid of any guidance or example from a normal mammal to support that leptin inhibits angiogenesis in adipose tissue one of the skill in the art would not know that leptin inhibits angiogenesis in adipose tissue of a normal mammal. It is noted to applicant that the specification on pages 27-28 recites Example 3, and not Example 7 (as argued in pg. 2 of the response) which discloses that leptin induces VEGF in preadipocytes significantly but not much in mature adipocytes. Even if leptin is angiostatic in mature adipocytes and angiogenic in preadipocyte, and if this model can be applied to a normal mammal, at best it suggests to one of the skill in the art that leptin is either angiogenic or it is angiostatic but it does not suggest to one of the skill in the art that leptin inhibits angiogenesis in adipose tissues of a normal mammal. Since the specification discloses that the administration of leptin in ob-/ mice inhibits angiogenesis in adipose tissue, the Examiner indicates that the claims drawn a method of inhibiting angiogenesis in ob-/ mice by administering leptin are allowable.